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The effect of exercise interventions on resting metabolic rate: a systematic review and meta-analysis.

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1. ABSTRACT

The systematic review and meta-analysis evaluated the effect of aerobic, resistance and combined exercise on RMR (kCal/day) and performed a methodological assessment of indirect calorimetry protocols within the included studies. Subgroup analyses included energy/diet restriction and body composition changes. Randomized control trials (RCTs), quasi – RCTs and cohort trials featuring a physical activity intervention of any form and duration excluding single exercise bouts were included. Participant exclusions included medical conditions impacting upon RMR, the elderly (≥65 years of age) or pregnant, lactating or post-menopausal women. The review was registered in the International Prospective Register of Systematic Reviews (CRD 42017058503). 1669 articles were identified; 22 were included in the qualitative analysis and 18 were meta-analysed. Exercise interventions (aerobic and resistance exercise combined) did not increase resting metabolic rate (mean difference (MD): 74.6 kcal/d [95% CI: -13.01, 161.33], P =0.10). While there was no effect of aerobic exercise on RMR (MD: 81.65 kcal/d [95% CI: -57.81, 221.10], P = 0.25), resistance exercise increased RMR compared to controls (MD: 96.17 kcal/d [95% CI: 45.17, 147.16], P = 0.0002). This systematic review effectively synthesises the effect of exercise interventions on RMR in comparison to controls; despite heterogenous methodologies and high risk of bias within included studies.

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2. KEYWORDS

Measurement, Metabolism, Nutrition, Physiology, Exercise.

3. INTRODUCTION

Human energy expenditure has three primary components: activity energy expenditure, resting metabolic rate (RMR) and dietary induced thermogenesis (DIT) [1]. The accurate measurement and interpretation of RMR is beneficial as it is a principal contributor to daily energy expenditure. In practice, this is usually measured by Indirect Calorimetry, a method that is 'indirect' as it measures airflow and the percentage of oxygen (O_2) and carbon dioxide (CO_2) to generate the respiratory exchange ratio (RER) which is subsequently converted to energy expended through known relationships [2, 3]. It is important for practitioners to understand how behaviours and lifestyle can impact on components of energy expenditure, in particular the effect of exercise on RMR is of interest as it has implications for health and sports performance. Despite this, there is a lack of agreement in the literature regarding the potential for exercise to modulate RMR in humans.

Previous studies have reported increases, decreases or no change in RMR as a result of chronic adaptations to endurance or resistance exercise programs [4-9]. These differences may be attributable to a range of factors. For example, changes in body composition directly impact RMR due to the relative energy contribution of different body tissues; fat-free mass is known to explain 25 - 70% of the variance in RMR and therefore gains and/or losses in skeletal muscle due to resistance or aerobic exercise can impact on RMR [10, 11]. As well, changes in dietary intake and/or energy expenditure with an exercise program will impact RMR and its interpretation [12]. In addition to these primary factors, other physiological and genetic factors contribute as exercise has the ability to impact thyroid status, protein turnover, circulating leptin [13], thermogenesis [14], β-adrenergic stimulation [15] and mitochondrial activity in the liver [16]. While understanding these factors is important for the interpretation of changes in RMR, equivocal changes in RMR as a response to exercise have also been

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attributed to sample size, differences in methodology - particularly the timing and technique of measurement - and the intensity and duration of exercise programs [17].

While Indirect Calorimetry is widely accepted as a valid and reliable method of determining RMR, high precision in the estimate of RMR is achieved when best-practice methodologies are employed [18, 19]. In short, several aspects of measurement must be standardised including familiarisation and/or acclimatisation with the measurement and the ventilated hood, test conditions, stimulant intake, food intake and physical activity prior to measurement, physiological state (e.g. illness, medications, altitude) and the method of measurement and analysis [18, 19]. The method has been used successfully in the general population and is regularly reported in studies examining the effects of exercise on whole body metabolism [20, 21]. However, it is currently unclear whether publications that report changes in RMR adhere to, and report, best practice protocols.

This systematic review synthesised evidence from experimental intervention studies that assessed the effect of exercise programs including resistance exercise or endurance/aerobic exercise on RMR to assess the primary research question 'what is the effect of aerobic, resistance and combined exercise training modalities on RMR (kCal/day) measured by indirect calorimetry in comparison to a control group?. In addition, secondary aims for this systematic review included 1) performing subgroup analyses assessing the impact of energy/diet restriction, changes in body weight and body composition on changes in RMR and 2) providing an overview of the methodologies reported in the included studies measurement of RMR and how these align with best practice guidelines. It is hypothesised that regular or prolonged exercise would have a measurable effect on RMR in accord with changes in body composition.

4. MATERIALS AND METHODS

This systematic review was conducted in line with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis: The PRISMA statement [22], and the guidelines of the Cochrane Handbook for Systematic Reviews and Interventions [23]. The methods including the eligibility criteria, search strategy, extraction process and analysis were pre-specified and documented in a protocol that was published in the International Prospective Register of Systematic Reviews (CRD42017058503) available at https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=58503.

4.1. Literature search

A literature search was performed in the electronic databases MEDLINE, EMBASE, CENTRAL and SPORTSDISCUS (from inception to July 22, 2018), using a combination of subject headings, free text terms and synonyms relevant to this review, in consultation with a systematic review search librarian (**Supplemental Table 1**). There was no date or language restriction in the search strategy non-English studies were translated and assessed against inclusion criteria. A multi-step search approach was taken to retrieve relevant studies through additional hand-searching. Two review authors (DS and JK) screened articles in a blinded, standardized manner, with disagreements in judgement resolved by consensus or a third reviewer (KMcKS).

4.2. Study selection

Search results were merged into reference management software Endnote (X8; Thomson Reuters) and de-duplicated prior to screening. Studies were included if they met all of the following criteria: 1) randomized controlled trial (RCT), cluster RCT, quasi-RCT, prospective cohort and retrospective cohort trials; 2) inclusion of adult participants (≥18 years of age); 3) intervention involving exercise and physical activity training; 4) inclusion of non-exercising control group as a comparator; 5) assessed resting metabolic rate (RMR) at the beginning and end of intervention using indirect calorimetry.

Studies involving populations with conditions impacting upon RMR - including medical conditions such as sepsis and thyroid conditions the elderly (≥65 years of age), or pregnant, lactating, or post-menopausal women were excluded. Studies involving the use of medications or known stimulants known to elevate RMR were also excluded [18, 19]. Eligible interventions included physical activity or training of any form (e.g. aerobic exercise, resistance training or concurrent training) of any duration, although studies involving a single (acute) exercise bout were excluded. Studies involving multifactorial interventions involving physical activity and dietary change were included if the dietary change delivered as the intervention also served as the non-exercising comparator.

The primary outcome was between-group differences in either RMR, resting energy expenditure or basal metabolic rate at the end of intervention, as well as changes from baseline. Studies were included only if they reported on the primary study outcome, as either between-group differences or changes from baseline.

4.3. Data extraction and management

Three reviewers (DS, JK and KMcKS) independently extracted the data from eligible studies, and one reviewer (KMcKS) determined the final extraction when there were differences or omissions. Data extracted included: study design (duration, location, details of ‘run-in’ periods); participant characteristics, intervention details (type of physical activity, intensity, duration and compliance); and other information including indirect calorimetry methodology used, body composition assessment method and change in body composition analysis.

For all pre-specified primary, secondary and exploratory outcome data, the mean, standard deviation (SD), standard error (SE) or 95% confidence intervals (CI) that were reported at end of intervention were extracted for analysis. Where studies involved multiple intervention groups involving different types of physical activity, data was extracted for each intervention for separate analysis. Where multiple intervention arms reported the same type of activity (for example two different aerobic activities) results were combined and compared against the control in one analysis.

Risk of bias was independently assessed by two reviewers (DS and JK) using Cochrane methodology [24] which assesses five domains of potential bias with each domain rated either low, unclear or high risk of bias. Disagreements in risk of bias between the two independent reviewers were resolved through discussion.

4.4. Statistical analysis

The overall treatment effect of physical activity on primary and secondary outcomes was calculated using the difference between either the end of intervention values or change scores for the intervention and comparator groups. Variance was calculated from the SD and SE of end of intervention values or change scores, or from the confidence intervals (CI) where these values were not available [25]. In crossover studies, the mean and SD, SE or CI of intervention and control periods were extracted and analyzed separately [26]. Where intervention endpoint data was unable to be obtained, the results were described narratively.

Meta-analysis was performed where outcomes were reported in at least two studies using Revman (Version 5.3; Cochrane Collaboration). Outcome data was converted to the same units prior to meta-analysis (kcal/day) and was reported as the mean difference (MD)[27]. A random-effects model was used to produce a pooled estimate of the MD, and the fixed-effects model was used to check for robustness and potential outliers. Inconsistencies between studies were assessed using the I^2 statistic, where significant heterogeneity was defined as $I^2 \geq 50\%$.

Post hoc subgroup analyses were undertaken for primary and secondary outcomes that were reported in at least two studies in each subgroup. Post hoc subgroup analyses included: intervention types (aerobic and resistance training), exercise-alone versus combined diet-exercise interventions, changes in total body mass (TBM) during the study period (increased; decreased; stable; and not reported). These were categorised (decreased, versus stable, versus increased) where a significant change in body composition was reported.

In studies including multiple, separate arms involving different exercise interventions, the interventions were pooled together for the overall meta-analysis, with a weighted average of the intervention arms and study variance calculated [28]. In the subgroup analyses exploring the effect of different intervention types on RMR, the interventions were analysed separately based on their respective intervention types

Significant outliers were determined by visual inspection as well as through a study-by-study sensitivity analysis, where each study was sequentially omitted, and the remaining data re-assessed. If a study contributed to over 30% heterogeneity (based on changes to the I^2 statistic) then it was removed from the analysis in the sensitivity analysis [27]. Funnel plots were generated for outcomes where at least 10 studies were included in the meta-analysis [29] and reporting bias detected by assessment of funnel plot asymmetry by visual inspection.

5. RESULTS

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The literature search identified 1669 articles; the PRISMA Diagram in Figure 1 summarises the results of the literature search. 22 studies were included in the qualitative analysis and 18 studies provided enough information to be included in the meta-analysis.

5.1. Study characteristics

The general characteristics of trials included in the systematic review are summarised in Table 1. A total of 822 participants were captured in 22 studies; with most including less than 45 participants with the exception of Scharhag-Rosenberger et al. [30], Frey-Hewitt et al. [31], Jennings et al. [32] and Gomersall et al. [33] which included 74, 85, 103 and 107 participants, respectively. One study by Hunter et al. [34] did not specify the exact number of participants but reported the inclusion of at least 140 participants. The meta-analysis included data from 392 participants and 270 controls. Most of the studies were a parallel study design except for one cross-over study design [35]. The majority of studies were conducted in overweight/obese populations that were predominantly sedentary [5, 31, 32, 34-44], two in type-2 diabetic populations [32, 40], one in a population with metabolic syndrome [37], several in predominantly normal-weight and/or healthy sedentary populations [17, 30, 33, 45-48] and one in active, healthy populations [20]. All studies captured were in adult populations, with several predominately focussing on females [5, 34, 36, 39, 42-44, 46, 48], males [17, 20, 31, 38, 41, 47], a combination of both [30, 32, 33, 35, 40, 45] or gender was not reported [37].

Several interventions were exercise only; with either a predominant focus on aerobic exercise [17, 31, 40], resistance exercise [5, 30, 35, 38, 46, 48] or a combination of both exercise modalities [32, 33]. Many studies used a combined dietary and exercise intervention; with four studies using predominantly aerobic exercise [36, 37, 45, 47], two in resistance exercise [20, 39] and five using a combination of both exercise modes [34, 41-44]. The shortest intervention was 10 days [47]; while several studies were conducted over 2-6 weeks [20, 33, 39, 40, 43]. The majority of interventions were conducted over 12 weeks [17, 36, 37, 41, 42, 44-46] while several longer interventions spanned 20-24 weeks [5, 32, 35, 38] and the longest study intervention was 12 months [31]. While some studies did not measure or report body composition assessments [33, 37]; the majority of studies used Dual-Energy X-Ray Absorptiometry (DEXA) [20, 34-36, 39, 40, 45, 48], anthropometry/skinfolds [30, 38, 43, 46], hydrostatic weighing, underwater weighing/air-displacement plethysmography [5, 17, 31, 41, 44, 47] or bio-electrical impedance (BIA) [32, 42].

5.2. Meta-analysis

Eighteen studies were able to be meta-analysed. Four studies were not included in the meta-analysis as they only presented data in graphs or with no means/variance reported [37, 42], did not contain specific participant numbers [34] or did not report outcome data in units that were able to be reliably converted for meta-analysis [30].

Across the 18 intervention studies pooled into meta-analysis, exercise (aerobic and resistance exercise combined) did not significantly increase RMR (MD: 74.16 kcal/day [95% CI: -13.01, 161.33], P =0.10; Figure 2). There was high heterogeneity (I^2 = 96 %); with two studies contributing as outliers [31, 36]. Neither study contributed over 30% toward the total heterogeneity, with 7% (21) and 22% (26), respectively. However, removal of these two studies from the analysis reduced the heterogeneity to 20%, and the overall finding became significant (MD: 61.45 kcal/day [95% CI: 27.46, 95.44], P=0.0004).

Aerobic exercise did not significantly increase RMR compared to the control group (MD: 81.65 kcal/day [95% CI: -57.81, 221.10], P = 0.25, Figure 2), however there was high heterogeneity (I^2 = 98%)Resistance exercise significantly increased RMR compared to the

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control group (MD: 96.17 kcal/day [95% CI: 45.17, 147.16], *P* = 0.0002; Figure 2) with minimal statistical heterogeneity ($I^2 = 0\%$).

5.3. Subgroup analyses

Subgroup analysis comparing the effects of exercise-only interventions with combined exercise and dietary interventions showed that showed that both types of interventions led to a similar effect, with neither exercise-only (MD: 46.79 kcal/day [95% CI: -9.52,103.09], *P* = 0.10, Figure 3) nor exercise and diet (MD: 74.16 kcal/day [95% CI: -13.01, 161.33], *P* = 0.12, Figure 3) subgroups having a significant effect on RMR.

Subgroup analysis comparing exercise intervention in individuals based on anthropometric changes in TBM had a significant effect on RMR. Studies that reported a stable body mass throughout the intervention period showed exercise increased RMR (MD: 66.17 kcal/day [95% CI: 2.95, 129.38], *P* =0.04, Figure 4). Studies that reported either an increase in body mass or failed to report on body mass, showed RMR was not different as it was just outside the P <0.05 pre-determined criteria (MD: 70.61 kcal/day [95% CI: -3.58,144.81] , *P* =0.06, Figure IV and MD: 89.27 kcal/day [95% CI: -3.20,181.74], *P* =0.06, Figure 4). There was no effect of exercise on RMR in studies that reported a decreased body mass (MD: 84.59kcal/day [95% CI: -77.37, 246.54], *P* =0.31, Figure 4).

5.4. Comparison of study methods

The methodologies that were used and reported for measuring RMR are summarised in Supplementary File 2. Of the studies that reported RMR methodology; several studies reported using a ventilated hood [17, 33, 40, 43-45, 47] and several used a mouthpiece with one-way valve/nose clip [31, 39, 46, 48]. Most studies reported measuring RMR for 30 – 45 minutes [5, 17, 20, 30, 32-34, 36, 39, 41, 45, 46]; with some reporting shorter durations of 10

– 25 minutes [31, 40, 42-44, 48] while others did not report RMR measurement duration [35, 37, 38, 47]. Many studies did not report acclimation or familiarisation to the test protocol but of the available data acclimation was undertaken between 15 - 30 minutes duration [5, 17, 31-34, 39-44, 46] While many studies did not report a fasting duration prior to measurement of RMR studies that provide detailed methods show participants were fasted 10 hours [41], 12 hours [17, 31-33, 39, 40, 43, 46] or overnight prior to commencing the test [20, 34, 48]. Some studies reported time in recovery/rest following a previous exercise bout; either 12 hours [31, 33, 47], 24 hours [30, 42], 36 hours [5], 48 hours [17, 32, 48] or 72 hours [35] – however most did not report the intensity or mode of the last exercise session. The RMR was typically derived from measurements of resting oxygen uptake (VO_2), carbon dioxide production (VCO_2) and RER (VCO_2/VO_2) using the Weir formula [49]. Some, but not all, studies reported the test environment and conditions during which the measurement was undertaken (e.g. thermo-neutral; low-light). RMR data was reported in a range of units e.g. mJ/d, kJ/d, kJ/min and was generally reported as an absolute change.

The studies reported several methods of body composition assessment including Dual-Energy X-Ray Absorptiometry [20, 35, 36, 39, 40, 45, 48], Hydrostatic weighing or Air-displacement plethysmography [5, 17, 31, 41, 44, 47], Bio-electrical impedance [32, 42] or skinfolds/anthropometry [30, 38, 43, 46]. Several studies reported TBM but did not report FFM [30, 38, 43, 46] and several studies did not report TBM or FFM [33, 37, 47].

5.5. Risk of Bias

The risk of bias was unclear for many of the studies for random sequence generation, allocation concealment, participant/personnel blinding and selective reporting (Supplementary File 3). The risk of bias was low for blinding of outcome assessment, moderate for incomplete outcome data and moderate-high for other bias.

22% of studies adequately reported random sequence generation to support a low risk of bias assessment and allocation concealment [30, 32, 33, 35, 48]. For all studies, the risk of bias for blinding of the participants to their condition was unclear and the risk of bias for blinding of the outcome was low. For incomplete outcome data; 22% of studies had a high risk of bias [34, 35, 38, 42, 43], 22% had an unclear risk of bias [5, 31, 36, 41, 45] and 55% had a low risk of bias [17, 20, 30, 32, 33, 37, 39, 40, 44, 46-48]. For selective reporting, 9% had low [30, 33], 86% had an unclear [5, 17, 20, 31, 32, 34-48]; while only one study had a high risk of bias [36] . Only a single study was judged as high risk of bias for 'other bias' [34] because it didn't report on participant numbers, with 32% of studies judged as low risk of bias [30-33, 38, 40, 47], with the remainder judged to be unclear.

6. DISCUSSION

The primary findings from the review were 1) resistance exercise significantly increased RMR in comparison to a control group as measured by indirect calorimetry, 2) aerobic exercise and exercise-combined (i.e. resistance exercise and aerobic exercise) did not significantly increased RMR in comparison to a control group, 3) a lack of comparable body composition assessment data meant it was unclear how changes in body composition interacted with changes in RMR and 4) while there were a large proportion of studies which did not report key aspects of their methodology that would represent best practice and/or there was inconsistency in methodology between studies, this meta-analysis only included studies with a control group thus limiting the impact of their methodological differences on the meta-analysis

The meta-analysis captured data from 392 participants and 270 controls (total 662 participants) and in large part addresses the inherent limitation of small-scale or single-arm

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studies. This systematic review provides new information to show a resistance exercise program has the capacity to increase RMR. A primary adaptation associated with resistance training is upregulation of anabolic processes within skeletal muscle resulting in hypertrophy and increased muscle cross sectional area [50]. It is generally well-accepted that increases in fat-free/lean mass and total body mass may induce an increase in RMR due to greater volume of metabolically active tissue, skeletal muscle remodelling and increasing the fat free-to-total body mass ratio [51-53]. Moreover, fat-free mass has been shown to make a substantial contribution (25– 70 %) to individual variations in RMR [10, 11]. While the findings of the meta-analysis support such a contention, the sub-analyses did not support a clear association between changes in body composition and RMR. Unfortunately, total body mass was not reported on all occasions and while some studies used body composition assessment measures that more accurately measure compartmental body mass (i.e. fat mass and fat-free mass) others, such as DEXA, used derived or predicted values to determine reported compartmental body mass. Moreover, there is an increasing awareness of the deficiencies in the 2-compartment (FFM and FM) profile of body composition in explaining variance in RMR and in RMR changes, and that the future may lie in an operational quantitative dynamic organ-system RMR model [54].

While the data clearly show resistance exercise is effective for increasing RMR, a similar outcome was not apparent for aerobic exercise. Interestingly, aerobic exercise has the capacity to induce modest hypertrophy but the effect may be dependent on the mode and intensity of aerobic exercise and the physical activity status of the participant [55]. In addition, our meta-analysis showed the overall effect of aerobic and resistance exercise combined on RMR was not significant. Therefore, we suggest the addition of higher quality, methodologically sound studies are warranted to better determine the effects of different exercise modalities on RMR. While no study contributed greater than 30% heterogeneity; two clear outliers reported a significant increase in RMR following aerobic exercise

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compared to a control group [31, 36]. As it was not explicitly stated - and the methodological reporting was broad - it was not clear whether the studies adhered to best-practice protocols for the measurement of RMR. Interestingly, when these studies were removed from the analysis there was a significant, positive effect of combined exercise modalities on RMR.

A potential confounding factor within the literature that may influence this meta-analysis is the effect of preceding exercise when study cohorts progress from sedentary to exercising status. Specifically, baseline RMR testing may be undertaken without preceding exercise while post-intervention testing may occur with limited recovery after the final exercise bout which may artificially inflate the measurement of RMR. It is important that studies follow best practice protocols which prescribe cessation from exercise or vigorous physical activity for a standardized period prior to the measurement of RMR. Compher et al. [18] recommend 2 hours of abstention from moderate aerobic exercise (Grade II – fair) and 14 hours for vigorous exercise (Grade III – limited) and Fullmer et al. [19] recommend 12-48 hours after light to vigorous intensity physical activity. As many of the participants were untrained and were potentially doing exercise that would generate post-exercise oxygen consumption (EPOC) and due to the potential for micro-trauma and repair of muscle damage, it has also been suggested that longer periods of abstinence up to 72 hours may be warranted [53]. Many studies in the current meta-analysis did not report abstinence from physical activity prior to the measurement of RMR. If exercise was performed in this time this could artificially inflate the measurement and thus the authors could conclude an effect of the exercise intervention on RMR; however as there was a methodologically-comparative control group in each study the overall effect in this meta-analysis would not be impacted. In addition, while our inclusion criteria allowed for interventions that both included or did not include dietary interventions, and energy balance is one consideration that may influence RMR independent of training [12], these were only included where the diet only intervention served as the control group.

The sub-analysis confirmed that the effect of exercise on RMR was similar between exercise-only and combined dietary-exercise studies.

The methodology characteristics table (Supplementary File 2) highlighted several gaps in the included study methodologies when compared to best practice guidelines. While many studies reported a fasting period in-line with best-practice guidelines, other areas of standardisation including familiarisation, time-of-day, room conditions, body position, the control for stimulants or supplements and physiological conditions (illness, medications) prior to measurement was minimal. Other key aspects of RMR methodology, including the calculation of steady-state and calibration procedures were not routinely reported despite being important aspects of evidence-based practice [18, 19]. The risk of bias was moderate-high for some of the studies. While most studies did not report random sequence generation or allocation concealment, this is difficult in small-scale studies that include an exercise intervention.

This systematic review and meta-analysis clearly shows that resistance exercise generates increases in resting metabolic rate while aerobic and combined resistance and aerobic exercise fail to induce a robust effect on changes in RMR. While some limitations of this systematic review have already been discussed, it should also be noted that number of observations can impact statistical significance and there were less resistance exercise studies. In addition, the overall effect had wide confidence intervals suggesting a high variability in data. The systematic review included exercise interventions of any type and duration, excluding single exercise bouts, and thus compared different study designs and methodologies. For example, while there was a clear effect of resistance exercise on RMR, differences in the type of resistance exercise and its' overarching aim (i.e. changes in power, strength or muscular endurance) were beyond the scope of this review. As well, the effect of exercise was most evident when total body mass remained stable during the intervention period, but lack of comparable data means it was unclear how changes in body composition interacted with changes in RMR. Despite this, a strength of this systematic review and meta-analysis is that it addresses the inherent limitation of small-scale or single-arm studies as it included a range of studies in comparison to control group. It is strongly recommended that future studies to adhere to best-practice protocols in the measurement of RMR and body composition assessment and to ensure that methodology is adequately reported to permit replication and appropriate interpretation [18, 19].

7. AUTHORSHIP CONTRIBUTION

KMS, NB and VC contributed to the study design concept and protocol. KMS, DS and JK contributed to the initial and updated literature search and screening, data extraction and risk of bias. KMS drafted the manuscript with contribution from DS and JK. All authors performed critical analysis and revision of manuscript and approved the final version.

8. ACKNOWLEDGMENTS

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9. CONFLICT OF INTEREST

Authors K. MacKenzie-Shalders, J.T. Kelly, D, So, V.G, Coffey & N.M. Byrne declare they have no conflicts of interest.

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11. REFERENCES

1. Levine, J.A., *Measurement of energy expenditure.* Public Health Nutrition, 2005. **8**(7A): p. 1123-32.
2. Levesey, G., *Estimation of energy expenditute, net carbohydrate utilization, and net fat oxidation and synthesis by indirect calorimetry : evaluation of errors with special referece to the detailed composition of fuels.* Am J Clin Nutr, 1988. **47**: p. 608-628.
3. Lusk, G., *Diet and Disease.* Am J Public Health (N Y), 1924. **14**(4): p. 297-301.
4. Lemmer, J.T., et al., *Effect of strength training on resting metabolic rate and physical activity: age and gender comparisons.* Medicine & Science in Sports & Exercise, 2001. **33**(4): p. 532-41.
5. Byrne, H.K. and J.H. Wilmore, *The effects of a 20-week exercise training program on resting metabolic rate in previously sedentary, moderately obese women.* Int J Sport Nutr Exerc Metab, 2001. **11**(1): p. 15-31.
6. Morio, B., et al., *Effects of 14 weeks of progressive endurance training on energy expenditure in elderly people.* British Journal of Nutrition, 1998. **80**(6): p. 511-9.
7. Ryan, A.S., et al., *Resistive training increases fat-free mass and maintains RMR despite weight loss in postmenopausal women.* Journal of Applied Physiology (1985), 1995. **79**(3): p. 818-23.
8. Lovelady, C.A., et al., *Effects of exercise on plasma lipids and metabolism of lactating women.* Medicine & Sciense in Sports & Exercise, 1995. **27**(1): p. 22-8.
9. Hunter, G.R., et al., *Increased Resting Energy Expenditure after 40 Minutes of Aerobic But Not Resistance Exercise.* OBESITY, 2006. **14**(11).
10. Silva, A.M., et al., *Changes in regional body composition explain increases in energy expenditure in elite junior basketball players over the season.* European Journal of Applied Physiology, 2012. **112**(7): p. 2727-37.
11. Westerterp, K.R., et al., *Long-term effect of physical activity on energy balance and body composition.* The British Journal of Nutrition, 1992. **68**(1): p. 21-30.
12. Broeder, C.E., et al., *The effects of either high-intensity resistance or endurance training on resting metabolic rate.* The American Journal of Clinical Nutrition, 1992. **55**(4): p. 802-10.
13. Fedewa, M.V., et al., *The Effect of Chronic Exercise Training on Leptin: A Systematic Review and Meta-Analysis of Randomized Controlled Trials.* Sports Medicine, 2018. **48**(6): p. 1437-1450.
14. Chung, N., et al., *Non-exercise activity thermogenesis (NEAT): a component of total daily energy expenditure.* J Exerc Nutrition Biochem, 2018. **22**(2): p. 23-30.
15. Zouhal, H., et al., *Catecholamines and the effects of exercise, training and gender.* Sports Medicine, 2008. **38**(5): p. 401-23.
16. Stevanović, J., et al., *Physical exercise and liver "fitness": Role of mitochondrial function and epigenetics-related mechanisms in non-alcoholic fatty liver disease.* Molecular Metabolism, 2020. **32**: p. 1-14.
17. Lee, M.G., et al., *Resting Metabolic Rate after Endurance Exercise Training.* Medicine & Science in Sports & Exercise, 2009. **41**(7): p. 1444-1451.
18. Compher, C., et al., *Best Practice Methods to Apply to Measurement of Resting Metabolic Rate in Adults: A Systematic Review.* Journal of the American Dietetic Association, 2006. **106**: p. 881-903.
19. Fullmer, S., et al., *Evidence Analysis Library Review of Best Practices for Performing Indirect Calorimetry in Healthy and Non–Critically Ill Individuals.* Journal of the Academy of Nutrition and Dietetics, 2015. **115**(9): p. 1417-1446.e2.
20. Arciero, P.J., et al., *Comparison of creatine ingestion and resistance training on energy expenditure and limb blood flow.* Metabolism: Clinical and Experimental, 2001. **50**(12): p. 1429-1434.
21. MacKenzie-Shalders, K.L., et al., *Are increases in skeletal muscle mass accompanied by changes to resting metabolic rate in rugby athletes over a pre-season training period?* European Journal of Sport Science, 2019: p. 1-8.
22. Moher, D., et al., *Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement.* Syst Rev, 2015. **4**: p. 1.

23. Higgins, J. and S. Green, *Cochrane handbook for systematic reviews of interventions*. 2011, Hoboken, New Jersey.: John Wiley & Sons.

24. Higgins, J. and D. Altman, *Assessing risk of bias in included studies*, in *Cochrane handbook for systematic reviews of interventions*, J. Higgins and S. Green, Editors. 2008, John Wiley & Sons.: Hoboken, New Jersey. p. 187-241.

25. Higgins, J., *Selecting studies and collecting data*, in *Cochrane handbook for systematic reviews of interventions.*, J. Higgins and S. Green, Editors. 2008, John Wiley & Sons: Hoboken, New Jersey. p. 151-85.

26. Elbourne, D.R., et al., *Meta-analyses involving cross-over trials: methodological issues.* Int J Epidemiol, 2002. **31**(1): p. 140-9.

27. Deeks, J.J., J.P. Higgins, and D.G. Altman, *Analysing data and undertaking meta-analyses*, in *Cochrane Handbook for Systematic Reviews of Interventions*, J.P. Higgins, et al., Editors. 2019, Cochrane. p. 241-284.

28. Higgins, J., J. Deeks, and D. Altman, *Special topics in statistics*, in *Cochrane handbook for systematic reviews of interventions*, J. Higgins and S. Green, Editors. 2008, John Wiley & Sons: Hoboken, New Jersey. p. 481–529.

29. Sterne, J., M. Egger, and D. Moher, *Addressing reporting biases*, in *Cochrane handbook for systematic reviews of interventions*, J. Higgins and S. Green, Editors. 2008, John Wiley & Sons: Hoboken, New Jersey. p. 297-333.

30. Scharhag-Rosenberger, F., et al., *Irisin Does Not Mediate Resistance Training-Induced Alterations in Resting Metabolic Rate.* Medicine & Science in Sports & Exercise, 2014. **46**(9): p. 1736-1743.

31. Frey-Hewitt, B., et al., *The effect of weight loss by dieting or exercise on resting metabolic rate in overweight men.* International Journal of Obesity, 1990. **14**(4): p. 327-334.

32. Jennings, A.E., et al., *The effect of exercise training on resting metabolic rate in type 2 diabetes mellitus.* Medicine and Science in Sports and Exercise, 2009. **41**(8): p. 1558-1565.

33. Gomersall, S.R., et al., *Testing the activitystat hypothesis: a randomised controlled trial.* BMC public health, 2016. **16**: p. 900.

34. Hunter, G., et al., *Exercise Training and Energy Expenditure following Weight Loss.* Medicine and science in sports and exercise, 2015. **47**(9): p. 1950-1957.

35. Kirk, E.P., et al., *Minimal resistance training improves daily energy expenditure and fat oxidation.* Medicine and Science in Sports and Exercise, 2009. **41**(5): p. 1122-1129.

36. Akbulut, G. and N. Rakiciogu, *The Effects of Diet and Physical Activity on Resting Metabolic Rate (RMR) Measured by Indirect Calorimetry, and Body Composition Assessment by Dual-Energy X-Ray Absorptiometry (DXA). / Diyet ve Fiziksel Aktivitenin İndirekt Kalorimetrik Yöntemle Ölçülen Dinlenme Metabolizma Hızı (DMH) ve Dual-Enerji X-ray Absorpsiyometresi (DXA) ile Ölçülen Vücut Bileşimine Etkisi.* Turkish Journal of Physical Medicine & Rehabilitation / Turkiye Fiziksel Tip ve Rehabilitasyon Dergisi, 2012. **58**(1): p. 1-8.

37. Bonfanti, N., et al., *Effect of two hypocaloric diets and their combination with physical exercise on Basal metabolic rate and body composition].* Nutricion Hospitalaria, 2014. **29**(5): p. 635-643.

38. Bonfante, I.L., et al., *Combined training, FNDC5/irisin levels and metabolic markers in obese men: A randomised controlled trial.* Eur J Sport Sci, 2017. **17**(5): p. 629-637.

39. Gornall, J. and R.G. Villani, *Short-term changes in body composition and metabolism with severe dieting and resistance exercise.* International Journal of Sport Nutrition, 1996. **6**(3): p. 285-294.

40. Karstoft, K., et al., *Resting Metabolic Rate Does Not Change in Response to Different Types of Training in Subjects with Type 2 Diabetes.* Front Endocrinol (Lausanne), 2017. **8**: p. 132.

41. Kraemer, W.J., et al., *Influence of exercise training on physiological and performance changes with weight loss in men.* Med Sci Sports Exerc, 1999. **31**(9): p. 1320-9.

42. Meckling, K.A. and R. Sherfey, *A randomized trial of a hypocaloric high-protein diet, with and without exercise, on weight loss, fitness, and markers of the Metabolic Syndrome in overweight and obese women.* Appl Physiol Nutr Metab, 2007. **32**(4): p. 743-52.

43. Rehová, I., et al., *Effects of intervention programs on changes in resting energy expenditure/vliv intervenčních programů na změny klidového.* Acta Universitatis Palackianae Olomucensis. Gymnica, 2007. **37**(4): p. 45-50.
44. Whatley, J.E., et al., *Does the amount of endurance exercise in combination with weight training and a very-low-energy diet affect resting metabolic rate and body composition?* American Journal of Clinical Nutrition, 1994. **59**(5): p. 1088-92.
45. Arciero, P.J., et al., *Increased dietary protein and combined high intensity aerobic and resistance exercise improves body fat distribution and cardiovascular risk factors.* Int J Sport Nutr Exerc Metab, 2006. **16**(4): p. 373-92.
46. Cullinen, K. and M. Caldwell, *Weight training increases fat-free mass and strength in untrained young women.* J Am Diet Assoc, 1998. **98**(4): p. 414-8.
47. Goran, M.I., et al., *Effects of increased energy intake and/or physical activity on energy expenditure in young healthy men.* J Appl Physiol (1985), 1994. **77**(1): p. 366-72.
48. Miller, T., et al., *Resistance Training Combined With Diet Decreases Body Fat While Preserving Lean Mass Independent of Resting Metabolic Rate: A Randomized Trial.* Int J Sport Nutr Exerc Metab, 2018. **28**(1): p. 46-54.
49. Weir, J.B., *New methods for calculating metabolic rate with special reference to protein metabolism.* Journal of Physiology, 1949. **109**(1-2): p. 1-9.
50. D'Antona, G., et al., *Skeletal muscle hypertrophy and structure and function of skeletal muscle fibres in male body builders.* The Journal of Physiology, 2006. **570**(3): p. 611-627.
51. ten Haaf, T. and P.J.M. Weijs, *Resting Energy Expenditure Prediction in Recreational Athletes of 18–35 Years: Confirmation of Cunningham Equation and an Improved Weight-Based Alternative.* PLoS ONE, 2014. **9**(10): p. e108460.
52. Jagim, A.R., et al., *The accuracy of resting metabolic rate prediction equations in athletes.* J Strength Cond Res, 2017.
53. Strasser, B., *Physical activity in obesity and metabolic syndrome.* 2013. **1281**(1): p. 141-159.
54. Heymsfield, S.B., et al., *Human energy expenditure: advances in organ-tissue prediction models.* Obesity Reviews, 2018. **19**(9): p. 1177-1188.
55. Konopka, A.R. and M.P. Harber, *Skeletal Muscle Hypertrophy After Aerobic Exercise Training.* Exercise and Sport Sciences Reviews, 2014. **42**(2): p. 53-61.

Figure Legends

Figure 1: Flow diagram of studies evaluated in the systematic review.

Figure 2: Forest plot of randomized controlled trials in adults comparing interventions involving exercise and physical activity training with non-exercising control group comparators. The overall effect of exercise and physical activity is presented (1.2.1). Additionally, sub-group effects based on the specific type of exercise training are also presented: aerobic (1.2.2) and resistance (1.2.3). Data are presented as means and SDs of RMR at the end of intervention. Effects of trials are presented as kilocalorie per day and MD (95% CI). CI, confidence interval; IV; inverse variance; MD, mean difference; RMR, resting metabolic rate; SD, standard deviation.

Figure 3: Forest plot of randomized controlled trials in adults comparing interventions involving exercise and physical activity training with non-exercising control group comparators. Studies are sub-grouped by whether the exercise and physical activity training was delivered alone (1.14.1) or in combination with dietary modifications (1.14.2). Data are presented as means and SDs of RMR at the end of intervention. Effects of trials are presented as kilocalorie per day and MD (95% CI). CI, confidence interval; IV; inverse variance; MD, mean difference; RMR, resting metabolic rate; SD, standard deviation.

Figure 4: Forest plot of randomized controlled trials in adults comparing interventions involving exercise and physical activity training with non-exercising control group comparators. Studies are sub-grouped based on the mean reported changes in total body mass of participants during the study period, categorised as: stable (1.6.1); increased (1.6.3); decreased (1.6.4); and not reported (1.6.6). Effects of trials are presented as kilocalorie per day and MD (95% CI). CI, confidence interval; IV; inverse variance; MD, mean difference; RMR, resting metabolic rate; SD, standard deviation.